NATIONAL MARROW DONOR PROGRAM®

Entrusted to operate the C.W. Bill Young Cell Transplantation Program,
including Be The Match Registry®

April 26, 2012

CDR Sheri Parker
Office of Naval Research (ONR 342)
875 N. Randolph St.
Arlington, VA 22203-1995

Subject: **Quarterly Performance/Technical Report of the National Marrow Donor Program®**

Reference: Grant Award #N00014-12-1-0142 between the Office of Naval Research and the National Marrow Donor Program

Dear Cdr. Parker:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of December 1, 2011 to March 31, 2012.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention at 612-362-3403 or at cabler@nmdp.org.

Sincerely,

Carla Abler-Erickson

Carla Abler-Erickson, MA
Sr. Contracts Representative

Enclosure: Quarterly Report with SF298

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14. ABSTRACT

1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation: Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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NATIONAL MARROW DONOR PROGRAM®

Creating Connections. Saving Lives.™

Grant Award N00014-12-1-0142

DEVELOPMENT OF MEDICAL TECHNOLOGY FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS

QUARTERLY PERFORMANCE / TECHNICAL REPORT

FOR

DECEMBER 01, 2011 to MARCH 31, 2012

PERIOD 1

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
Minneapolis, MN 55413
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QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

December 01, 2011 through March 31, 2012

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IIA. Contingency Preparedness – Objective 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians	
IIA.1 Task 1: Secure Interest of Transplant Physicians	**Period 1 Activity:** • Initiated coordination for Advanced Medical Radiation Response training to be held on July 16-17, 2012 at the Radiation Emergency Assistance Center and Training Site in Oakridge, TN for up to 25 RITN center staff
IIA.1 Task 2: GCSF in Radiation Exposure	**Period 1 Activity:** • No activity this period.
IIA.1 Task 3: Patient Assessment Guidelines and System Enhancements	**Period 1 Activity:** • No activity this period.
IIA.1 Task 4: National Data Collection Model – The activity under this Task has moved to IID.1 Task1.	
IIA. Contingency Preparedness – Objective 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.	

IIA.2 Task 1: Contingency Response Network	**Period 1 Activity:**
	• Began the process of coordinating the site assessments of RITN transplant centers
	  o Assessments will review critical areas necessary for responding to a mass casualty incident with marrow toxic injuries
	  o Areas include: victim processing, outpatient treatment of victims, inpatient treatment of victims, coordination with region, state or federal agencies; documentation review
	• As of April 23, 2012 RITN consists of: 47 – transplant centers, 6 - donor centers, and 7 - cord blood banks
	• As part of the continued work on expansion of transplant centers participating in RITN, invitations were sent to 21 hospitals; 9 of these have expressed interest and are reviewing the participation agreement and annual required tasks

	• RITN Medical Advisor activity; Dr. Weinstock participated in the following activities supporting the Radiation Injury Treatment Network: o He co-authored: ▪ a manuscript in press for Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science ▪ a manuscript in press for Leukemia on response to the Fukushima Daiichi nuclear power plant incident ▪ a manuscript submitted to Lancet on response to radiation incidents o He assisted with the 2012 update of the RITN Medical Grand Rounds Course o He assisted with the publication of the RITN Concept-of-Operations document o He assisted with the development of the 2012 RITN Table-Top Exercise o He represented RITN at a meeting with BARDA in February 2012 o He represented RITN at a meeting with the American Hospital Association in February 2012 o He was invited to speak at the BARDA symposium on blood products in November 2012 o He was invited to speak at the National Burn-bed strategy meeting in March 2012 • Conducted the monthly RITN Center conference call to review task completion status and allow a venue for centers to talk to peers
IIA.2 Task 2: Sibling Typing Standard Operating Procedures	**Period 1 Activity:** • No activity this period.

IIA. Contingency Preparedness – Objective 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
IIA.3 Task 1: I.S. Disaster Recovery – This Task is closed.	
IIA.3 Task 2: Critical Facility and Staff Related Functions	**Period 1 Activity:** • Initiated the annual review of each of the 21 NMDP departments critical task list and assigned personnel • Began planning for the 2012 Business Continuity Plan Exercise
IIB. Rapid Identification of Matched Donors – Objective 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.	
IIB.1 Task 1: Increase Registry Diversity	**Period 1 Activity:** • Four contracted HLA testing laboratories performed HLA-A, B, DRB1 typing, two laboratories performed HLA-A, B, C, DRB1, DQB1 typing, on a total of 70,810 newly recruited donors. o Blind quality control testing error rate was 0.14%, meeting the project requirement of ≤ 2.0%. o On-time testing completion rate was 99.0%, meeting the project requirement of a minimum of 90% of typing results reported within 14 days of shipment of samples. • In the process of typing and confirming rare alleles, certain patterns became evident that indicated when a sample was likely incorrectly reported. These patterns included 1.) allele reported in multiple race groups or allele reported in race group that differed from the IMGT submission, 2.) allele reported with a second rare or uncommon allele, and 3.) allele frequently reported before 2004 and less frequently reported after that date. Using these guidelines, uncommon alleles in 205 samples stored at the repository were selected for typing.
IIB.1 Task 2: Evaluate HLA-DRB1 High Resolution typing – This Task is closed.	
IIB.1 Task 3: Evaluate HLA-C Typing of Donors – This Task is closed	
IIB.1 Task 4: Evaluate Buccal Swabs	**Period 1 Activity:** • No activity this period.

IIB.1 Task 5: Enhancing HLA Data for Selected Donors – This Task is closed.	
IIB.1 Task 6: Maintain a Quality Control Program	**Period 1 Activity:** • A working group was established to formulate a pilot plan to supplement the blind QC program with swabs donated by registry volunteers. Work continues to establish the protocol for 1) identification and contact of potential donors, 2) establishing expected typing, and 3) incorporation into sample shipments. The goals of this project are to develop a cost-effective method to increase the number of unique lots that would be presented to laboratories and to increase the diversity of HLA types represented. • Sixty-five samples from the Research Repository were selected for incorporation into the NMDP QC program and will be sent for cell culture/initiation/expansion. These samples ensure that the NMDP QC inventory has complete coverage of all Common and Well-Documented (CWD) alleles with a count greater than 1:10,000 and all but 14 CWD alleles with a minimum count of 25 by sequenced based typing methods, and expand alleles that were depleted to an n of 1.
IIB. Rapid Identification of Matched Donors – Objective 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.	
IIB.2 Task 1: Collection of Primary Data	**Period 1 Activity:** • No activity this period.
IIB.2 Task 2: Validation of Logic of Primary Data – This Task is closed.	
IIB.2 Task 3: Reinterpretation of Primary Data – The activity under this Task has moved to Task IIB2 Task 4.	
IIB.2 Task 4: Genotype Lists & Matching Algorithm	**Period 1 Activity:** • No activity this period.

IIB. Rapid Identification of Matched Donors – Objective 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.	
IIB.3 Task 1: Phase I of EM Haplotype Logic	**Period 1 Activity:** • No activity this period.
IIB.3 Task 2: Enhancement of EM Algorithm	**Period 1 Activity:** • Began processing of BMDW data in preparation for 5-locus BMDW haplotype frequency study. • Continued development of a manuscript describing 6-locus haplotype frequency data utilized in HapLogic III. • Calculated 5-locus high-resolution haplotype frequency for Canadian populations by detailed race • Developed simulation framework for testing methods of generating synthetic haplotype frequencies to lower sampling error in population frequencies and submitted abstract to WMDA International Donor Registry Conference. • Launched project to automate quarterly haplotype frequency updates to HapLogic.
IIB.3 Task 3: Optimal Registry Size Analysis	**Period 1 Activity:** • No activity this period.
IIB.3 Task 4: Target Under- Repre-sented Phenotypes	**Period 1 Activity:** • Presented hypotheses to the BRAGG committee for approval. Began working with ESRI consultants to develop modeling of concordance maps. • Met with John November (Assistant Professor, Department of Ecology and Evolutionary Biology University of California-Los Angeles) to discuss approaches for modeling HLA concordance. • Prepared a manuscript describing the HLA imputation method, analysis and validation framework and reporting validation results. Manuscript currently being reviewed for submission. • Drafted study design and protocol documents for an Ancestry Questionnaire Pilot (AQP) study to introduce enhancements to the ancestry questionnaire used by donors to join the registry and correlate

	the results with genetic ancestry and HLA information.
IIB.3 Task 5: Bioinformatics Web Site	**Period 1 Activity:** • No activity this period
IIB.3 Task 6: Consultants to Improve Algorithm	**Period 1 Activity:** • No activity this period.
IIB.3 Task 7: Population Genetics – The activity under this Task has moved to IIB.3.2.	
IIB.3 Task 8: Haplotype Matching – The activity under this Task has moved to IIB.3.2.	
IIB.3 Task 9: Global Haplotype/Benchmark – The activity under this Task has moved to IIB.3.3.	
IIB. Rapid Identification of Matched Donors – Objective 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.	
IIB.4 Task 1: Expand Network Communications – This Task is closed.	
IIB.4 Task 2: Central Contingency Management	**Period 1 Activity:** **NIH Transplant Center** • NMDP provided support for donor/cord blood unit identification, selection and collection for the NIH intramural unrelated donor transplant program. Activity in the last quarter was as follows: o 7 formal searches o 41 donor confirmatory typing blood sample and IDM testing requests o 7 cord blood unit confirmatory typing requests o 3 cord blood units o 1 marrow and 6 PBSC collections

IIB.4 Task 3: Benchmarking Analysis	**Period 1 Activity:** • No activity this period.
IIB.4 Task 4: Expand Capabilities of Collection and Apheresis Centers – This Task is closed.	
IIC. Immunogenetic Studies – Objective 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.	
IIC.1 Task 1: Donor Recipient Pair Project	**Period 1 Activity:** • No activity this period.
IIC. Immunogenetic Studies – Objective 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.	
IIC.2 Task 1: Analysis of non-HLA loci	**Period 1 Activity:** • No activity this period.
IIC.2 Task 2: Related Pairs Research Repository – This Task is closed.	
IIC.2 Task 3: CIBMTR Integration – This Task is closed.	
IID. Clinical Research in Transplantation – Objective 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.	
IID.1 Task 1: Observational Research, Clinical Trials and NIH Transplant Center	**Period 1 Activity:** **Prospective Studies; RCI BMT** • During this reporting period staff initiated discussions and planning related to the following two projects: a) comprehensive system for management of activities and studies within the SRG portfolio and b) centralized system to coordinate operational and administrative activities this clinical trial management system. **Information Technology: FormsNet and AGNIS** FormsNet

	Additional accomplishments were made in delivering new functionality, improving data quality, data capture and data reporting through the CIBMTR IT suite of applications. A technical release was completed to lay the foundation for the FormsNet application upgrade planned in late 2012. An additional release was completed that increased data quality and improved the efficiency in preparing data for analysis for Observational Studies. A release was implemented to automate monitoring of a clinical trial, thereby increasing efficiency FormsNet 3 is a little over half way through the development phase and the project is on track for a Nov 2012 implementation. The use of the Agile methodology approach is working very well, providing frequent opportunities for the business to view and test the deliverables/system. **AGNIS** • Released support of form 2000 in the AGNIS Publisher (3/27/12) • Testing of forms 2018 and 2118 (Lymphoma Disease forms) • Production submission available for EBMT to submit forms 2400 and 2804. Working to expand 2400 diseases for submission and EBMT center data sharing agreements • Continue to support EBMT efforts for bulk form submission • Stanford has submitted an error free 2400 in development. • RemedyMD is submitting forms 2900, 2804, and 2450 in production for University of Utah. Development efforts to submit other forms and to retrieve forms underway. • 20 StemSoft centers retrieving data.
IID.1 Task 2: Research with NMDP Donors – The activity under this Task has moved to IID.1.1.	
IID.1 Task 3: Expand Immuno-biology Research	**Period 1 Activity:** • No activity this period.

ACRONYM LIST

AABB	American Association of Blood Banks	HML	Histoimmunogenetics Mark-up Language
AFA	African American	HR	High Resolution
AGNIS	A Growable Network Information System	HRSA	Health Resources and Services Administration
AML	Acute Myelogenous Leukemia	HSC	Hematopoietic Stem Cell
ABD	Antigen Binding Domain	IBWC	Immunobiology Working Committee
API	Asian Pacific Islander	IDM	Infectious Disease Markers
AQP	Ancestry Questionnaire Pilot	IHWG	International Histocompatibility Working Group
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IPR	Immunobiology Project Results
ASBMT	American Society for Blood and Marrow Transplantation	ICRHER	International Consortium for Research on Health Effects of Radiation
ASHI	American Society for Histocompatibility and Immunogenetics	IND	Investigational New Drug
B-LCLs	B-Lymphoblastoid Cell Lines	IS	Information Services
BARDA	Biomedical Advanced Research and Development Authority	IT	Information Technology
BBMT	Biology of Blood and Marrow Transplant	IRB	Institutional Review Board
BCP	Business Continuity Plan	JCAHO	Joint Commission on Accreditation of Healthcare Organizations
BCPeX	Business Continuity Plan Exercise	KIR	Killer Immunoglobulin-like Receptor
BMCC	Bone Marrow Coordinating Center	MDACC	MD Anderson Cancer Center
BMDW	Bone Marrow Donors Worldwide	MDS	Myelodysplastic Syndrome
BMT	Bone Marrow Transplantation	MHC	Major Histocompatibility Complex
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MICA	MHC Class I-Like Molecule, Chain A
BODI	Business Objects Data Integrator	MICB	MHC Class I-Like Molecule, Chain B
BRT	Basic Radiation Training	MKE	Milwaukee
C&A	Certification and Accreditation	MRD	Minimal Residual Disease
CAU	Caucasian	MSKCC	Memorial Sloan-Kettering Cancer Center
CBMTG	Canadian Blood and Marrow Transplant Group	MSP	Minneapolis

CBB	Cord Blood Bank	MUD	Matched Unrelated Donor
CBC	Congressional Black Caucus	NAC	Nuclear Accident Committee
CBS	Canadian Blood Service	NCBM	National Conference of Black Mayors
CBU	Cord Blood Unit	NCI	National Cancer Institute
CHTC	Certified Hematopoietic Transplant Coordinator	NEMO	N-locus Expectation-Maximization using Oligonucleotide typing data
CIBMTR	Center for International Blood & Marrow Transplant Research	NHLBI	National Heart Lung and Blood Institute
CIT	CIBMTR Information Technology	NIH	National Institutes of Health
CLIA	Clinical Laboratory Improvement Amendment	NIMS	National Incident Management System
CME	Continuing Medical Education	NK	Natural Killer
CMF	Community Matching Funds	NLE	National Level Exercise
COG	Children's Oncology Group	NMDP	National Marrow Donor Program
CREG	Cross Reactive Groups	NRP	National Response Plan
CSS	Center Support Services	NST	Non-myeloablative Allergenic Stem Cell Transplantation
CT	Confirmatory Testing	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CTA	Clinical Trial Application	OIT	Office of Information Technology
CWD	Common and Well Documented		
DC	Donor Center	OMB	Office of Management and Budget
DHHS-ASPR	Department of Health and Human Service – Assistant Secretary Preparedness and Response	ONR	Office of Naval Research
DIY	Do it yourself	P2P	Peer-to-Peer
DKMS	Deutsche Knochenmarkspenderdatei	PBMC	Peripheral Blood Mononuclear Cells
DMSO	Dimethylsulphoxide	PBSC	Peripheral Blood Stem Cell
DoD	Department of Defense	PCR	Polymerase Chain Reaction
DHHS-ASPR	Department of Health and Human Services – Assistant Secretary for Preparedness and Response	PSA	Public Service Announcement
DNA	Deoxyribonucleic Acid	QC	Quality control

DR	Disaster Recovery	RCC	Renal Cell Carcinoma
D/R	Donor/Recipient	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
EBMT	European Group for Blood and Marrow Transplantation	REAC/TS	Radiation Emergency Assistance Center/Training Site
EDC	Electronic Data Capture	RFP	Request for Proposal
EFI	European Federation of Immunogenetics	RFQ	Request for Quotation
EM	Expectation Maximization	RG	Recruitment Group
EMDIS	European Marrow Donor Information System	RITN	Radiation Injury Treatment Network
ENS	Emergency Notification System	SBT	Sequence Based Typing
ERSI	Environment Remote Sensing Institute	SCTOD	Stem Cell Therapeutics Outcome Database
FBI	Federal Bureau of Investigation	SG	Sample Group
FDA	Food and Drug Administration	SLW	STAR Link® Web
FDR	Fund Drive Request	SSA	Search Strategy Advice
FLOCK	Flow Cytometry Analysis Component	SSO	Sequence Specific Oligonucleotide
Fst	Fixation Index	SSP	Sequence Specific Primers
GETS	Government Emergency Telecommunications Service	SSOP	Sequence Specific Oligonucleotide Probes
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	STAR®	Search, Tracking and Registry
GIS	Geographic Information System	TC	Transplant Center
GvHD	Graft vs. Host Disease	TED	Transplant Essential Data
HCS	HealthCare Standard	TNC	Total Nucleated Cell
HCT	Hematopoietic Cell Transplantation	TSA	Transportation Security Agency
HEPP	Hospital Emergency Preparedness Program	UI	User Interface
HHQ	Health History Questionnaire	UML	Unified Modeling Language
HHS	Health and Human Services	URD	Unrelated Donor
HIPAA	Health Insurance Portability and Accountability Act	WGA	Whole Genome Amplification
HIS	Hispanic	WMDA	World Marrow Donor Association
HLA	Human Leukocyte Antigen	WU	Work-up